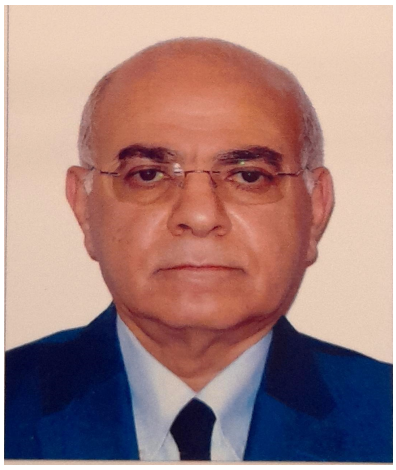

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Present Academic Rank and Position

- Professor, Head of Biochemistry Dept., Faculty of Pharmacy, Ahram Canadian University, Cairo, Egypt. December 2023 - present.

Previous Academic Ranks and Positions

- Associate Consultant, Mayo Clinic Comprehensive Cancer Center, Rochester, MN, USA.
- Assistant Professor, Department of Molecular Pharmacology and Experimental Therapeutics, Mayo Clinic School of Medicine, Rochester, MN, USA.
- Assistant Professor, Department of Clinical Pharmacology and Toxicology, University of Alabama at Birmingham (UAB), Birmingham, Alabama, USA.
- Research Instructor, Department of Clinical Pharmacology and Toxicology, University of Alabama at Birmingham (UAB), Birmingham, Alabama, USA.
- Associate Professor, Department of Biochemistry, Faculty of Medicine El-Minia University, El-Minia, Egypt.
- Lecturer of Biochemistry, Department of Biochemistry, Faculty of Medicine El-Minia University, El-Minia, Egypt.
- Assistant Lecturer of Biochemistry, Department of Biochemistry, Faculty of Medicine El-Minia University, El-Minia, Egypt.
- Medical Analysis Specialist, Endocrinology and Maternal Biochemistry Unit, Department of Obstetrics and Gynecology, Faculty of Medicine, Cairo University Hospitals, Egypt.

EDUCATION

- **Bachelor** of Pharmacy and Pharmaceutical Sciences, Faculty of Pharmacy, Cairo University, Cairo, Egypt (05/1976).
- **Master's** Degree of Pharmaceutical Sciences in Biochemistry, Faculty of Pharmacy, Cairo University, Cairo, Egypt (07/1984).
- **Doctorate** (PhD) of Pharmaceutical Sciences in Biochemistry, Faculty of Pharmacy, Cairo University, Cairo, Egypt (05/1991).
- **Fellowship in Molecular Biology**, Biochemistry Department, University of South (USA), Mobile, Alabama, USA (06/1999).
- **Fellowship in Molecular Biology**, Vision Science Research Center, University of Alabama at Birmingham (UAB), Birmingham, Alabama, USA, (11/2001).
- **Foreign Pharmacy Graduate Equivalency Exam (FPGEE),** National Association of Boards of Pharmacy, USA (2010).
- **Foreign Pharmacy Graduate Examination** Certificate (**FPGEC**)**,** National Association of Boards of Pharmacy-USA (2011).

MEDICAL LICENSURE

- National Registry of Certified Chemists (NRCC) **(**Board Certified Lab Director License), USA.
- Minnesota State Board of Pharmacy (Internship license), USA.
- Egyptian National Board of Pharmacy Practice.
- Egyptian National Board of Medical Analysis Specialists.

PROFESSIONAL MEMBERSHIPS

- American Association for Cancer Research (**AACR**); American Society for Clinical Pharmacology and Therapeutics (**ASCPT**); American Society of Clinical Oncology (**ASCO**); American Society of Human Genetics (**ASHG**).

EDITORIAL ACTIVITIES:

- Acted as a reviewer for the Journals of Clinical Oncology (JCO), Clinical Cancer Research (CCR), Cancer Research (CR), Pharmacogenetics and Genomics, The Pharmacogenomics Journal and the Journal of Human Mutation.
- Acted as the secretary for the Arab Journal of laboratory medicine for five years.

EDUCATIONAL ACTIVITIES

Teaching Activities: Teaching undergraduate & postgraduate Biochemistry courses for medical students. Teaching Hormones and Endocrine Regulation, Molecular Basis of Cancer, Genetic & Predisposition to Cancer to Medical students.

Professional Experience:

- Teaching undergraduate and postgraduate Biochemistry courses to medical students.
- Teaching Molecular cancer genetics.
- Mentoring of graduate students, fellows, Masters, and PhD students.
- Training of fellows, postdocs and technicians on Molecular biology techniques and methodologies.
- Technology implementation. Management of Laboratory Staff and Workload management.
- Direct, perform and manage Translational Cancer Research /investigations. This included study and experimental design of protocols, preparation and processing of human biospecimens (whole blood, plasma, serum, frozen and formalin-fixed paraffin-embedded [FFPE] tissue, fine needle aspirates and buccal smears) accrued from patients populations, for downstream application like high throughput genetic and biochemical analysis.
- Writing protocols for investigational translational studies and experimental design for human Bio-specimen collection; sample processing, storage and data analysis and interpretation.
- Directing and supervising clinical laboratory investigational studies, data analysis and interpretation and software evaluation.
- Development of several methods for the detection of molecular genetic defects in several genes associated with resistance and response to chemotherapy in cancer patients.
- Grant Writing, Author manuscripts and book chapters. Presentation of data in conferences and seminars.
- Establish Collaboration with Industry and academia / Universities.
- Supervising the execution of grants aims and writing grant's progress reports for funding authorities.
- Management of Department administrative responsibilities and Strategic planning.
- Performing and supervising Genetic analysis and screening of patients' samples recruited in clinical trials for epigenetic and genetic mutations and aberrations.
- Direct, perform and manages Translational Cancer Research. Study design. Experimental design. Staff management and leadership.
- Acted as a reviewer for Extramural grants.

- Acted as reviewer for reputable peer reviewed scientific journals.
- Development of a production facility for Molecular Assay Panels as well as the establishment of Quality control (QC) and Quality Assessment (QA) protocols and standard operating procedures (SOP) for the production of these molecular panels following CLIA and COLA guidelines and regulations. These panels included molecular assays for the diagnosis of patients with Upper respiratory, Urinary tract, Wound and Ear, nose and throat, infections in addition to other new panels that were in preparation for production (antibiotic resistance, sexually transmitted diseases and others). The 96 well plate maps for the different molecular panels were designed according to clinical relevance and reimbursement plans of the different health insurance entities and state policies. Molecular assay panels were produced in 96 well plate formats using an Eppendorf Liquid handler system 5075. I designed all the procedures for the Eppendorf Liquid handler system to run all the molecular panels, in the required numbers and format. Production also included the design and development of Validation and Calibration molecular panels for the validation and calibration of the PCR machines utilized in RT-QPCR of the different molecular assay panels – this included Lower limit of detection (LLOD) and Calibration molecular assay panels.

Other Professional Experiences:

- Thesis Committee Member of Graduate Students for Masters and Ph.D. Degree.
- Scientific Consultation for Adherex Company 2006-2007.
- Collaboration with industry (Qiagen, Inc.) for beta testing of new molecular biology product (Whole genome Amplification kits and Epitect kits for the Bisulfite modification of genomic DNA).
- New technology evaluation and feasibility study assessment for implementation and purchase.
- Scientific technical consultation for engineering team responsible for the design of the pharmacogenetics and genomics laboratory for our group in Mayo Clinic, Rochester, MN.
- Interview and evaluation of professionals selected as candidates for faculty positions in Mayo Clinic, Rochester, MN.
- Reviewer of intramural grant funding application in prostate scientific program of research excellence (Spore) in Mayo Clinic.

Code	JOB RELATED TRAINING
01EDIV228	Respectful Communication at Work 280646
01EDIV216	Communicating Across Styles 280355
52PHST2010	Infectious Agents 2010, Training for New and Current Physicians/Scientists 299315
1.00E+66	Project Management 280401
2ECMEAEAD	Analyzing Exon Array Data Using Partek GS Software 277025
2ECMEUPGS	Using Partek GS Software for Data Analysis and Visualization 277023
2ECMEIPGS	Introduction to Partek GS Software 277021
28EMR2009	Privacy Policy - Electronic Access to Protected Health Information 265059
52PHST2009	Infection Prevention and Control - 2009 Annual Training 265102
29MTPPHS01	Mayo Training Program - Protecting Human Subjects 257890
28PRIV2008	Protecting Confidentiality: Where's the Risk? 255141
28COI	Conflict of Interest Tutorial 255177
51EPSP2009	Emergency Preparedness Physician/ Scientists 2009 Training 255434
02PML140	Module IA 217232
52PHST2008	Infection Prevention and Control - 2008 Annual Training 231203
28REGINV07	Integrity & Compliance Program Education
52PMASTER	Infection Control Education for Physicians/Scientists 231225
28EFFCERT	Effort Certification 231323
51EPS2008	Emergency Preparedness 2008 Training 231118
28HIPC01	HIPAA Privacy and Security Online Course 228984
52NHT2008	Infection Prevention and Control - 2008 New Hire Training 229520
51EPSV2007	Emergency Preparedness Video 2007 217836
52PHST2007	Infection Control - 2007 Annual Training 214999
52PMASTER	Infection Control - Education for Physicians/Scientists 211947
57NEO180 NEO	Part 2 - Follow-Up 190916
06CP3000	Skin Cancer: Catch It Before It Catches You 199771
28INTPR01	Intellectual Property 200602
29IRBE IRBe	Demonstration and Learning Session 193451
29MTPPHS01	Mayo Training Program - Protecting Human Subjects 198563
01NEO150	New Employee Orientation 195714
28HIPC01	HIPAA Privacy and Security Online Course 196180
51RMS2007	Radioactive Materials 2007 Training 196417
51RMSN2007	Radiation Safety-Nuclear Medicine 2007 Training 196421
51RADO4001	Radioactive Materials - Access/Security 196415
51RADO4002	Radioactive Materials - Laboratory 196416
51RADO4003	Radioactive Materials - Nuclear Medicine 196420
01EDIV228	Respectful Communication at Work 280646

Mentoring of Students:

Name/ Affiliation	Study Title/Thesis	Date
Adam Lee, PhD Student Dept. of Pharmacology and Toxicology, University of Alabama at Birmingham, (UAB), Birmingham, AL.	Dihydropyrimidine Dehydrogenase Deficiency: Impact of Pharmacogenetics on 5-Fluorouracil Therapy. *Clin Adv Hem Oncol. 2004. 2 (8):527-532.* Methylation of the DPYD Promoter Down Regulates the Expression of Dihydropyrimidine Dehydrogenase (DPD) Enzyme; Potential Importance in DPD Deficient Cancer Patients - *AACR 96th Annual Meeting 2005 (LBA-10657- AACR)*.	2002-2009
Holly Reed, PhD Student Department of Pharmacology and Toxicology, University of Alabama at Birmingham, (UAB), Birmingham, AL.	Genetic And Epigenetic Regulation of Dihydropyrimidinase and Beta-Ureidpropionase in Fluoropyrimidine Catabolic Pathway. *Pharmacogenetics and Genomics. 2007; 17(11); pp 973-987.* Genetic Regulation of Beta-Ureidopropionase and Its Possible Implication in Altered Uracil Catabolism. *Pharmacogenetics and Genomics. 2008; 18(1); pp 25-35.*	2004-2008
Danijela Djordjevic Visiting Masters Student, School of Pharmacy, Univ. of Vienna, Austria.	Genetic and Epigenetic Regulation of Epidermal Growth Factor Receptor in Non Small Cell Lung Carcinoma.	2005-2006
Cornelia Hofmeyer Visiting Masters Student School of Pharmacy, Univ. of Vienna, Austria.	Simultaneous Detection of Variable Number Tandem Repeats, Single Nucleotide Polymorphisms and Allelic Imbalance in Thymidylate Synthase Gene Enhancer Region using Denaturing High Performance Liquid Chromatography. *Anal Biochem. 2004 Nov 15; 334 (2): 276-83.*	2003-2004
Yoshihiro Okamoto, PhD Visiting Scientist School of Pharmacy Meijo University, Tempaku-ku, Nagoya Japan.	Genotyping for Dihydropyrimidine Dehydrogenase (DPD) Deficiency following Fatal 5-Fluorouracil (5-FU) Toxicity; - Denaturing High Performance Liquid Chromatography (DHPLC) Analysis of Archival Tissue. *University of Alabama at Birmingham, Comprehensive Cancer Center, Annual Research Retreat 2002; 204A.* - A Semiautomated, Rapid, High Throughput Denaturing High Performance Liquid Chromatography (DHPLC) Method for Screening for Mutations Associated with Dihydropyrimidine Dehydrogenase (DPD) Deficiency. *Proc Am Assoc for Can Res 2002; 43:1595a.* - A High-Throughput Denaturing High-Performance Liquid Chromatography Method for the Identification of Variant Alleles Associated with Dihydropyrimidine Dehydrogenase Deficiency. *Anal Biochem 2002; 306 (1):63-73*. - Denaturing High Performance Liquid Chromatography (DHPLC)	2001-2002

	Analysis of the DPYD Gene in Patients with Lethal 5-Fluorouracil (5-FU) Toxicity. *Clin Cancer Res 2003; 9:3021- 3028.*	
S. EL-Laban Doctorate Student Medical School, El-Minia University, Egypt.	Dialysis Arthropathy: A Study of the Relation between Haemodialysis, Dialysis Associated Arthropathies and Associated Biochemical Changes. *Arab J Lab Med. 1996; 22(2):219-237*.	1994-1996
A. Mounir, master's degree Student Medical School, El-Minia University, Egypt.	The Effect of Occurrence of New Pregnancy on Unit Composition of Milk in Already Lactating Mothers.	1994-1996
E. Abdel-Fattah master's degree Student, Medical School, El-Minia University, Egypt.	Corroborative Study on Some Hormonal and Exogenous Factors Affecting Skeletal Age at the Epiphyseal Planes of the Upper Limb.	1994-1996
H. Shawki Doctorate Student Medical School, El-Minia University, Egypt.	Dysfunctional Uterine Bleeding: A Study of Endometrial Prostacyclin and Sex Steroid Hormones in Association with the Ultrastructure of Endometrial Vasculature. *Bull Egypt Soc Physiol Sci. 1995; 15(1): 41-54.*	1993-1995
A.B. Kamel Master's degree Student, Medical School, El-Minia University, Egypt.	The Endocrinological Patterns in Patients with Polycystic Ovary Disease. The Use of Biochemical Ratios. *Bull Egypt Soc Physiol Sci. 1995; 15(1):55-74*.	1993-1995
T. El-Amawy Doctorate Student, Medical School, El-Minia University, Egypt.	Steroid Hormones and Gonadotropin Concentrations in Infertile Men with Varicocele and Severe Oligozoospermia. *Arab J Lab Med. 1996; 22(2): 67-82.*	1992-1995
W. Abdel-Wahab Master Degree Student, Medical School, El-Minia University, Egypt.	Serum Procollagen III and Serum Laminin P1 in Childhood Acute Rheumatic Fever. *The New Egyptian Journal of Medicine 1994; 10:3.*	1992-1994
A.R. Mohie-Eldin Doctorate Student, Medical School, El-Minia University, Egypt.	Atrial Natriuretic Peptide, Aldosterone Plasma Rennin Activity and Prolactin in Hypertensive Disorders of Pregnancy. *Medical Journal of Cairo University. 1993; 61:4.*	1991-1993

Collaboration on Translational Clinical Trials and Studies:

Clinical Trials:

- **MC064G**: **A Pharmacogenetic-Based Phase I Trial of Irinotecan, 5-Fluorouracil, and Leucovorin (FOLFIRI) in Patients with Advanced Gastrointestinal Cancer.** Study Chair: Robert R. McWilliams, M.D, Study Co-chairs: Matthew P. Goetz, M.D(MCR, Oncology); Charles Erlichman, M.D. (MCR, Oncology); **Hany Ezzeldin, Ph.D.** (MCR, Translational component); Robert Diasio, M.D. (MCR, Translational component). Statistician: Rui Qin, Ph.D.

- **MC083D: Phase I/II study of LBH589 and Letrozole in post-menopausal women with basal-like (triple negative) or aromatase refractory metastatic breast cancer.** Study Chair: Winston Tan, M.D.; Study Co-Chairs: Edith A. Perez, M.D.; **Hany Ezzeldin, PhD**; Zhiguo Zhang, PhD; Ayman Noreddin, PhD; Statistician: Betsy LaPlant, MS; Brooke Fridley, PhD.

- **09-05-056-B: Investigation of Genetic Determinants of Capecitabine-Related Chemotherapy Toxicity.** (Univ. of Chicago). Study was approved by the TBCRC. Study Chair: Peter H. O'Donnell (Univ. of Chicago). Role in this study: **Hany Ezzeldin, Ph.D.** (Mayo Clinic Rochester, Translational component).

- **N0147: A Randomized Phase III Trial of Oxaliplatin (OXAL) Plus 5-Fluorouracil (5-F/Leucovorin (CF) with or without Cetuximab (C225) after Curative Resection for Patients with Stage III Colon Cancer. North Central Cancer Treatment Group.** Study Chairs: Steven R. Alberts, M.D. (Research Base) * Translational Component: **Hany Ezzeldin, Ph.D.**/ Robert Diasio, MD

Collaboration with Industry

- **Determination of the molecular basis of response to Vorinostat alone and in combination with 5-fluorouracil in colorectal cancer cell line models**. This study is performed in collaboration with ***Merck Pharmaceutical*** Company. The purpose of this study is to investigate whether vorinostat potentiates Pro-apoptotic effects of 5-FU in colon cancer cells; whether anti-proliferative effects of vorinostat and 5-FU are similar in non-metastatic, metastatic and 5-FU refractory colon cancer cells; whether vorinostat alone or in combination with 5-FU exert anti-proliferative effects by down-regulating the gene expression of *DPD* and *TS* involved in the 5-FU catabolic and anabolic pathways, respectively. **Role in this study**: Study design, supervision of molecular studies and data analysis.

Molecular Cancer Studies in collaboration with colleagues in Mayo Clinic:

- **Study Title: The Identification of Molecular Signatures Predictive of Response to Chemotherapy (5-FU) and Disease-Free Survival in Colorectal Cancer Patients. (IRB#09-002351).**

Specific Aims:

Aim 1: Determination of genome wide methylation, gene expression, and miRNA expression in stage III colorectal cancer patients and the association of these genomic signatures with disease free survival (DFS) and 5-FU related toxicities.

Aim 2: Validation of SNPs previously identified by our lab and others in genes regulating the pyrimidine catabolic and anabolic pathway.

Aim 3: The integration of the examined gene expression, differential methylation, miRNA and SNPs using statistical and bioinformatics tools for the identification of molecular signatures predictive of patients response to 5-FU, and 5-FU related toxicities, as well as DFS.

- **Study Title: CpG Island Methylator Phenotype in Primary Glioblastoma Multiforme Sensitive and Resistant to Temozolomide and Radiation Therapy as an Independent Molecular Marker of Response and Tumor Progression.**

Study performed in collaboration with Dr. Jann Sarkaria, MD (Brain Tumor Spore).

SPECIFIC AIMS

In this application we proposed the identification of a distinct molecular epigenetic signature characteristic of primary GBM tumors sensitive and resistant to Temozolomide/ Radiation therapy (TMZ/RT), as an independent molecular marker of response and tumor Progression.

Specific Aim 1: Determination of genome wide methylation status in primary GBM tumors sensitive and resistant to TMZ/RT.

Specific Aim 2: Determination of quantitative CpG site specific methylation signals in CpG islands of differentially methylated genes identified in specific aim 1 and in DNA satellite repeats Sat1 and Sat 2, in GBM tumors sensitive and resistant to TMZ/RT.

Study Title: The Role of Epigenetic Variation in the Modulation of Tumor Response to Chemotherapy. Study collaborators: Dr. Jann Sarkaria, MD (Brain Tumor Spore, Mayo Clinic), Dr. Hany Ezzeldin, PHD (Mayo Clinic-Translational Component) and Dr. Ayman Noreddin, Ph.D., (University of Minnesota, Hollow fiber 3D culture system).

Specific Aim 1: The Determination of epigenetic molecular signatures characteristic of GBM tumors sensitive and resistant to Temozolomide chemotherapy.

Specific Aim 2: The validation of a 3-D GBM tumor simulating model in predicting tumor response to chemotherapy following epigenetic modulation of GBM tumor molecular signatures.

Previous Research Grant Support:

Role	Grant Type, Name, Number and Brief Description	Date
Co-investigator	**NIH/NCI: 1R01 CA 62164** **Genetic Polymorphism of Dihydropyrimidine Dehydrogenase.** This grant examined the mechanism by which mutations produce DPD deficiency, attempted to identify and characterize transcriptional regulatory elements of the human DPYD gene and develop new phenotypic and genotypic tests for diagnosing the pharmacogenetic syndrome of DPD deficiency.	December 2001– November 2006
Co-investigator	**NIH/NCI: 5 R01 CA 085381-05** **Molecular Approach in Predicting 5-Fluorouracil (5-FU) Efficacy.** The long term objective of this study was to examine if a pharmacogenomic approach can be used to predict response and/or toxicity in patients with stage III colorectal cancer to the chemotherapy drug 5-Fluorouracil (5-FU).	July 24, 2001 – June 30, 2007
Co-investigator	Industry Grant: **Adherex Technologies Inc** This grant supported a preclinical study of the biochemical modulation of 5-FU by Eniluracil exploring a potential mechanism explaining why earlier clinical (Phase III) studies of a 5-FU/Eniluracil combination was inferior compared to 5-FU/Leucovorin.	September 01, 2005 – April 30th, 2009

Co-investigator	**NIH/NCI: 1 R01 CA 116964-01A1: Screening for Decreased 5-Fluorouracil Catabolism**. This grant supports the development of a breath test to evaluate DPD enzyme activity which will enable physicians to individualize therapy for newly diagnosed cancer patients prior to 5-Fluorouracil chemotherapy.	August 31, 2006 – July 31, 2011
Co-investigator	**Proteomics & Epi-Genetics of Anion-transport-Network.** Study in collaboration with International Research Staff Exchange Scheme (IRSES). (Markus Paulmichel: PI); Role in this study: Responsible for the Translational Epigenomic component. Translational Component: Quantitative Determination of CpG Island Methylator Phenotype (CIMP).	International Research Staff Exchange Scheme (IRSES)

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Publications:

1. Igor V. Peshenko1, Elena V. Olshevskaya1, Suxia Yao, **Hany H. Ezzeldin**, Steven J. Pittler, Alexander, M. Dizhoor1.Activation of Retinal Guanylyl Cyclase RetGC1 by GCAP1: Stoichiometry of Binding and the Effect of New LCA-Related Mutations. Biochemistry. 2010 Feb 2; 49(4):709-17.
2. **Hany H Ezzeldin**, Edward P Acosta, Lori K Mattison, Jeanne Fourie, Anil Modak and Robert B Diasio: 13C-5-FU breath test current status and future directions: a comprehensive review. J. Breath Res. 3 (2009) 047002 (12pp).
3. Ma X, **Ezzeldin HH,** Diasio RB. Histone deacetylase inhibitors: current status and overview of recent clinical trials. Drugs. 2009; 69(14); pp. 1911-34.
4. **Ezzeldin HH**, Diasio RB. Predicting Fluorouracil Toxicity: Can We Finally Do it? J Clin Oncology. 2008; 26(13): 2008-2.
5. **Ezzeldin HH**. Challenges in Pharmacogenetic Testing. 2008 AACR Education Book. 2008
6. Thomas HR, **Ezzeldin H**, Guarcello V, Mattison LK, Fridley BL and Diasio RB: Genetic Regulation of Beta-Ureidopropionase and Its Possible Implication in Altered Uracil Catabolism. Pharmacogenetics and Genomics. 2008; 18(1); pp 25-35.
7. Thomas HR, **Ezzeldin H**, Guarcello V, Mattison LK, Fridley BL and Diasio RB: Genetic Regulation of Dihydropyrimidinase and Its Possible Implication in Altered Uracil Catabolism. Pharmacogenetics and Genomics. 2007; 17(11); pp 973-987.
8. Saif MW, **Ezzeldin H**, Vance K, Sellers S, Diasio RB. DPYD*2A mutation: the most common mutation associated with DPD deficiency. Cancer Chemother Pharmacol. 2007; 60(4): 503-7.

9. Saif MW, Mattison L, Carollo T, **Ezzeldin H**, Diasio RB. Dihydropyrimidine dehydrogenase deficiency in an Indian population. Cancer Chemother Pharmacol. 2006; 58(3): 396-401.
10. **Ezzeldin HH,** Diasio RB. Genetic testing in cancer therapeutics. Clin Cancer Res.2006; 12(14 Pt 1): 4137-41.
11. Yu J, McLeod HL, **Ezzeldin HH**, Diasio RB. Methylation of the DPYD promoter and dihydropyrimidine dehydrogenase deficiency. Clin Cancer Res. 2006; 12(12):3864; author reply 3864.
12. **Ezzeldin HH,** Lee AM, Mattison LK, Diasio RB. Methylation of the DPYD Promoter: an alternative mechanism for dihydropyrimidine dehydrogenase deficiency in cancer patients. Clin Cancer Res. 2005; 11(24 Pt 1): 8699-705.
13. **Ezzeldin H**, Hoffmayer C, Soong R, Johnson MR, Lee A, Heslin M, Diasio R. Simultaneous detection of variable number tandem repeats, single nucleotide polymorphisms, and allelic imbalance in the thymidylate synthase gene enhancer region using denaturing high-performance liquid chromatography. Anal Biochem. 2004;334(2): 276-83.
14. **Ezzeldin H**., Diasio RB. Dihydropyrimidine dehydrogenase deficiency, a pharmacogenetic syndrome associated with potentially life-threatening toxicity following 5-fluorouracil administration. Clin Colorectal Cancer. 2004; 4(3):181-9.
15. Lee A, **Ezzeldin H**, Fourie J, Diasio R. Dihydropyrimidine dehydrogenase deficiency: impact of pharmacogenetics on 5-Fluorouracil therapy. Clin Adv Hematol Oncol. 2004; 2(8): 527-532.
16. Mattison LK, **Ezzeldin H**, Carpenter M, Modak A, Johnson MR, Diasio RB. Rapid identification of dihydropyrimidine dehydrogenase deficiency by using a novel 2-13C-uracil breath test. Clin Cancer Res. 2004; 10 (8):2652-8.
17. **Ezzeldin H,** Johnson MR, Okamoto Y, Diasio RB. Denaturing high performance liquid chromatography (DHPLC) analysis of the DPYD gene in patients with lethal 5-fluorouracil (5-FU) toxicity. Clin Cancer Res. 2003; 9(8):3021-8.
18. Koenekoop RK, Fishman GA, Iannaccone A, **Ezzeldin H**, Ciccarelli ML, Baldi A, Sunness JS, Lotery AJ, Jablonski MM, Pittler SJ, Maumenee I. Electroretinographic abnormalities in parents of patients with leber congenital amaurosis who have heterozygous GUCY2D mutations. Arch Ophthalmol. 2002; 120(10):1325-30.
19. **Ezzeldin H**, Okamoto Y, Johnson MR, Diasio RB. A high-throughput denaturing high-performance liquid chromatography method for the identification of variant alleles associated with dihydropyrimidine dehydrogenase deficiency. Anal Biochem. 2002; 306(1): 63-73.
20. Simovich MJ, Miller B, **Ezzeldin H**, Kirkland BT, McLeod G, Fulmer C, Nathans J, Jacobson SG, Pittler SJ. Four novel mutations in the RPE65 gene in patients with Leber congenital amaurosis. Hum Mutat. 2001; 18(2):164.
21. El-Sadek W, **Ezzeldin H.** The effect of renal failure and hemodialysis on the neuromuscular blocking actions of mivacurium and plasma choline esterase activity. Egyptian J Anaesthesia. 1998; 14:1.
22. Shaarawy M, El-Mallah SY, **Ezzeldin H,** Aref AI. Choice of reliable biochemical markers for assessment of bone remodeling in postmenopausal osteoporosis. Menopause. 1997; 4 (4):212-218.
23. Sharaf AA, **Ezzeldin H**, Eissa M, Kamel BA. The endocrinological patterns in patients with polycystic ovary disease. The use of biochemical ratios. Bull Egypt Soc Physiol Sci. 1995; 15(1):55-74.
24. Kafafi SM, Montasser M, **Ezzeldin H**, Hamid KA, El-Heny M, Gaber S, Shawki H. Dysfunctional uterine bleeding: a study of endometrial prostacyclin and sex steroid hormones in association with the ultrastructure of endometrial vasculature. Bull Egypt Soc Physiol Sci. 1995; 15(1): 41-54.
25. Abdel A, Al FH, Zein S, Saleh SM, Wahab WA, **Ezzeldin H,** Hegazy A. Serum procollagen III and serum laminin P1 in childhood acute rheumatic fever. The New Egyptian Journal of Medicine 1994; 10:3.
26. Lotfi AH, **Ezzeldin H.** Markers of endothelial injury in preeclampsia. J Biomed Sci Ther. 1994; 10:3.
27. Khattab MAE, Wahab AA, Salam ASE, Khoriba AM, **Ezzeldin H.** Osteocalcin and calcitonin in renal failure. The Egyptian Journal of Internal Medicine. 1994; 2:4.

28. Salem HT, Kafafy SM, Moftah HA, Sharaf AA, El-Gindy E, **Ezzeldin H,** Mohie-Eldin AR. Atrial natriuretic peptide, aldosterone, plasma rennin activity and prolactin in hypertensive disorders of pregnancy. Medical Journal of Cairo University. 1993; 61:4.
29. Abd El, Hafez FH, Said SZ, Saleh SM, **Ezzeldin H.** Serum insulin and C-peptide in children acute viral hepatitis. Journal of Arab Child. 1993; 4:2.
30. Saleh SM, Said SZ, **Ezzeldin H,** El-Sherif MA. Effect of protein energy malnutrition (PEM) on blood glucose and insulin homeostasis. J Arab Child. 1993; 4:2.
31. Shaarawy M, Omar S, Hamdy MA, **Ezzeldin H.** The diagnostic value of certain biochemical tumor markers in cases of cancer breast. Arab J Lab Med. 1984; 10:147-164.
32. Said SZ, Saleh SM, **Ezzeldin H**, Salem SA, El-Sherif MA. Serum fructoseamine in children with acute viral hepatitis. The New Egyptian Journal of Medicine. 1992; 7:2.

Book Chapters

1. **Ezzeldin H**, Diasio RB. Pharmacogenetics and Cancer Chemotherapy. In Budman DR, Calvert H, and Rowinsky E (eds): Handbook of Anticancer Drug Development. Lippincott Williams and Wilkins (Pubs), Wolters Kluwer Co, Philadelphia, 2003, 25; 343-378.

Selected Abstracts

1. **H. H. Ezzeldin**, A. M. Lee, G. J. Kitange, J. N. Sarkaria, R. B. Diasio. CpG island methylator phenotype as an independent molecular marker of response and tumor progression in chemotherapy/ radiation treated Glioblastoma Multiforme (GBM). ASCO-NCI-EORTC Annual Meeting on Molecular Markers in Cancer 2008-AB-50203-ASCOMM.
2. M. B. Lustberg, T. Bekaii-Saab, R. Diasio, **H. Ezzeldin**, S. L. Starrett, G. Otterson, M. Villlona. Phase II and pharmacogenetic study of docetaxel (D) and capecitabine (C) in chemonaive non-small cell lung cancer (NSCLC) patients (pts). 2008 American Society of Clinical Oncology. ASCO-AB-36298-ASCOAM.
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Research Interests and Plans

My interest in personalized medicine started with studies examining the molecular basis of toxicity secondary to treatment with 5-fluorouracil. My research on colorectal cancer involved the pharmacogenetics and epigenetics of molecular mechanisms regulating flouropyrimidine metabolizing enzymes and response to treatment. For the past several years I focused on investigating the molecular basis of deficient uracil catabolic enzymes involved in the elimination of approximately 85% of administered dose of 5-Fluorouracil. I investigated the genetic and epigenetic regulation of dihydropyrimidine dehydrogenase, the rate limiting enzyme in fluoropyrimidine catabolism [Anal Biochem. 2002; 306(1): 63-73], [Clin Cancer Res. 2005; 11(24 Pt 1): 8699-705] as well as enzymes down stream of dihydropyrimidine dehydrogenase, Dihydropyrimidinase [Pharmacogenetics and Genomics. 2007; 17(11); pp 973- 987], and Beta-ureidopropionase [Pharmacogenetics and Genomics. 2008; 18(1); pp 25-35].

My interest in understanding the molecular basis of interindividual variability in response and toxicity to chemotherapeutic drugs has been equally distributed between the identification of diagnostic and prognostic molecular signatures of response to treatment and the development of molecular tests capable of predicting patients' at risk of developing severe life threatening toxicity prior to the administration of chemotherapy. My research in molecular testing of patients resulted in the development of four rapid genetic screening methods and one phenotypic screening test. Tests for the detection of known and unidentified sequence variants included genetic screening methods for 1) dihydropyrimidine dehydrogenase, 2) Dihydropyrimidinase and 3) Beta-ureidopropionase genes using denaturing high performance liquid chromatography methods. This technique is capable of rapidly screening the entire dihydropyrimidine dehydrogenase gene for known and unknown sequence variants as well as differentiating between homozygous and heterozygous sequence variants [Anal Biochem 2002; 306 (1): 63- 73]. These methods identify patients with sequence variants commonly associated with decreased uracil catabolism and toxicity following the administration of 5-FU. 4) Additionally, I developed a method that allowed the simultaneous detection of the number of variable tandem repeats, Loss of heterozygosity, and mutations in the Thymidylate Synthase gene promoter enhancer region [Anal Biochem. 2004 Nov 15; 334 (2): 276-83]. The Thymidylate Synthase gene is associated with resistance to fluoropyrimidine treatment in cancer patients. These studies might contribute to safety label changes in package inserts for fluoropyrimidines as well as the development of diagnostic assays capable of identifying uracil deficient individuals prior to treatment. I have also contributed to the development of a phenotypic oral uracil breath test (UraBT) for the detection of uracil catabolic deficiency in cancer patients scheduled to receive a fluoropyrimidine treatment [Clin Cancer Res. 2004;10 (8):2652-8] (pending for FDA approval).

My research interest expanded to investigating the molecular determinants of response & resistance to Temozolomide treatment in glioblastoma (GBM) patients' xenografts and cancer stem cells (CSC). GBM is a fatal malignancy, with an average overall survival of approximately 12 months. Although Temozolomide treatment has marginally improved overall survival, recurrent resistant tumors remain a major problem with mostly unfavorable clinical outcome. GBM CSC has been implicated in chemo-resistance as well as local recurrence and metastasis. Targeting this cell population through the development of therapeutics that disrupt signaling pathways essential to CSC self-renewal and proliferation may provide an attractive strategy for inhibiting tumor growth and promoting tumor cell differentiation into non-tumorigenic progeny. This approach which is in contrast to the first- and second-line chemotherapy agents which failed in eliminating CSC as evidenced by local recurrence and metastasis could be more successful in eradicating residual disease and improve patients' outcome. The recent success of epigenetic therapy in treatment of different hematological malignancies drawing clinical benefits to patients and significantly increasing their OS and quality of life; in addition to recent reports indicating the presence of GBM CSC molecular subtypes (Neural, Proneural, Classical and mesenchymal) that could be predictive of treatment outcome, has encouraged me to initiate molecular studies to 1) identify Molecular subtypes characteristic of tumor xenografts and matched CSC obtained from GBM patients; 2) Selectively inhibit signaling pathways (e.g., Notch, Wnt, PARP and EGFR pathways were implicated in cancer and in response to treatment) in CSC neurospheres, and, 3) The identification of new therapeutic targets following epigenetic modulation that could allow the use of alternative treatment regimens capable of inhibiting CSC self-renewal and proliferation. We propose that the identification of comparable molecular subtypes (Proneural, Classical and mesenchymal) in GBM tumor xenografts and matched GBM CSC neurospheres could predict therapeutic response and could allow the design of successful targeted therapies to improve glioma therapy. In these studies fresh frozen tumor xenograft tissues, CSC neurospheres and tumor xenografts cell cultures are utilized. The experimental design includes multiple complementary approaches. The **first**, interrogates tumor xenografts and matched CSC using whole genome gene expression, whole genome miRNA expression (Illumina-BeadChip miRNA array) and whole genome methylation (Illumina-Infinium Methylation 27 Beadchip array). This is followed by the integration of these platforms using bioinformatics tools and network mapping to identify molecular subtypes, signatures and potential new therapeutic targets. The **second** approach targets the genes and pathways identified through bioinformatics analysis and network mapping through siRNA experiments and the use of monoclonal antibodies recently developed to selectively target gene pathways these monoclonal antibodies are available through collaborators. The **third** is the epigenetic modulation of resistant tumor xenografts and CSC in cultures using demethylating agents and histone deacetylases inhibitors HDACi (selective & pan HDACi) followed by treatment using different therapeutic agents (first line treatment and alternative treatments) followed by assessment of CSC response to treatment in comparison to tumor xenografts in culture. Multiple molecular biology techniques and high throughput genomic platforms will be utilized including Mass ARRAY in combination with the high throughput MALDI-TOF mass spectrometry which offers a suite of quantitative and qualitative applications for molecular testing of pathways at the genotyping, gene expression and CpG site specific methylation levels.

My long-term objective is personalized/individualized medicine through the identification of pharmacogenetic and Pharmaco-epigenetic molecular signatures associated with the impact of chemotherapy on target phenotype. My future research directions will focus on the identification of new therapeutic targets and more effective drug formulations through the implementation of nanoparticle technology that could allow the development of more effective therapies in cancer treatment. This targeted molecular approach could greatly decrease the health care costs and significantly improve the patients' standard of care and quality of life.

Statement of Teaching Philosophy

My interest and experience in teaching biochemistry to medical students as an assistant lecturer, lecturer, assistant professor, and professor has significantly contributed to my increased interest in teaching the pharmacogenetics and pharmaco-epigenetics of Cancer chemotherapy, personalized medicine and cancer genetics. This interest started early with my research studies examining the molecular basis of toxicity secondary to treatment with 5-fluorouracil in colorectal cancer patients, and with my involvement in clinical translational research. My postdoctoral fellowship training on molecular biology techniques and the gained technical expertise allowed me to combine the theoretical basic science with translational research. Through my teaching career I realized that the integration of basic sciences, biochemistry, pharmacology, physiology and microbiology is crucial for understanding the complex molecular mechanisms associated with interindividual variability in response to therapy. I believe that this integration makes abstract concepts and dry material more relatable to my students, cements the basic principles of science and helps them relate to a discipline that touches the lives of all people. My teaching philosophy could be summarized in the following bullet points:

- **T**ailor the subject matter in a clear & organized manner to suit the students' need, demonstrating a sincere interest & enthusiasm for the subject, and providing a balanced learning environment as an effective medium to impact the students in a two-way process.
- **E**ngage critical thinking skills through the use of case studies to help in explaining the differences in response to the same standard dose of a chemotherapeutic agent. Understanding interindividual genetic and molecular variability is the key to pharmacogenetic and genomic rules of drug engagement. Throughout my learning history and teaching career I realized that this approach helped to better deliver the principles and concepts of pharmacogenetics and genomics.
- **A**ttempt to remain current. Reflecting on the recent advances in pharmacogenetics and genomics, which is becoming an integral part of medical education, keeps the student excited and connected with this hot and rapidly growing discipline. A practical approach would give the students an opportunity to present a 15-minute lecture on the pharmacogenetics of a drug, in which they are interested, followed by discussions. This gives the students the opportunity to

interact, improve their communication skills and teaches them how to prepare and present articles from peer-reviewed scientific journals.

- **C**ommunicate and listen; teachers shape who we are as individuals and thus will impact how we learn.
- **H**ighlight the importance of class discussions and encourage students to clarify their understanding of the subject. The realization that teaching is a two-way process requires building bridges of mutual trust.
- **I**ntegration of knowledge from different scientific fields. Pharmacology, biochemistry, pharmacogenetics and Pharmaco-epigenetics is more than the study of how substances interact with biological systems or how biological systems functions or react differently to biological agents and drugs. I believe that the integration of knowledge from these disciplines offers a unique perspective on the coming era of "Personalized Medicine" in the quest to prevent and treat disease.
- **N**ote the important points raised by the students through discussions. This will help in adding, updating, clarifying or modifying the curriculum if needed. This stems from my credence that both teachers and students contribute significantly and equally to the mutual learning process.
- **G**ain students' trust by creating a stimulating learning environment that encourages them to interact with me and with one another through formal and informal discussions. I believe that this is an integral part of knowing how to interact with students/partners in education.

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Appendix: (pdf docs for selected manuscripts).


01- Activation of Retinal Guanylyl Cycl


02-13C-5-FU breath test current status an


03-Histone deacetylase inhibitors


04- Predicting 5FU Toxicity-Can We Final


05- Challenges in Pharmacogenomic Te


06- Genetic regulation of beta-ure


07- Genetic regulation of dihydro


08- DPYD2A mutation the most co


09- Dihydropyrimidine de


10- Genetic Testing in Cancer Therapeutic


11-Methylation of the DPYD Promoter-L


12- Methylation of the DPYD Promoter.p


13- Simultaneous detection of variable r


14- Dihydropyrimidine D


15- Dihydropyrimidine D


16- Rapid Identification of Dihyc


17- Denaturing High Performance Liquid Chic


18-Electroretinograp abnormalities in p


19- A High-Throughput Der


20- Four Novel Mutations in the RPE6


22- Choice of Reliable Biochemical I


23- The endocrinological patte


24- Dysfunctional Uterine Bleeding A st


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